weight under other treatment, and at the beginning of October I was again requested to try tuberculin as a last resort. On October 5th the index was 1.2, and I injected $\frac{1}{1000}$ mg. The child immediately improved in spirits and weight, but on October 13th had a severe gastro-enteric attack and nearly died. Since then she has steadily improved on fortnightly doses of $\frac{1}{1000}$ mg., and her weight rose from 1 st. 11 lb. on October 26th to 2 st. 7 lb. 6 oz. on December 30th. From January 11th, however, she again began to lose weight, and on February 2nd a tuberculous mastoiditis was discovered and treated by operation. Tuberculin was continued, the wound healed rapidly, and her weight, which had sunk to 2 st. 6 lb. on February 19th, had risen to 2 st. 8 lb. by February 26th, and the child continues to improve.

Estimations of the opsonic index, 14. Injections, 9.

CASE IV.

A. G., aged 6 years, wasted and anaemic, showed some enlargement of glands, and peritonitis of the dry variety. The history dates from January, 1906. The opsonic index before injection was 0.8, the first injection ($\frac{1}{1000}$ mg.) was given on November 13th, and subsequent inoculations at intervals of about two weeks. The weight on November 11th was 1 st. 13 lb. 6 oz., steadily rising to 2 st. 5 lb. 5 oz. by February 17th, the child being now rosy and fairly plump. Treatment continues.

Opsonic indices, 9. Injections, 6.

CASE V.

J. T., 9 years of age, was brought to me for wasting on August 20th. I considered the child tuberculous, but a careful examination discovered no lesion. Ten days later he returned with abdominal pain and swelling, and there was free fluid present in the abdomen. I admitted him to hospital, and on September 5th there appeared also a small effusion in the left pleural sac. The opsonic index before injection was 0.86; the first injection ($\frac{1}{1000}$ mg.) was given on September 5th, and by September 19th both the pleural and peritoneal effusions had disappeared, and he was gaining weight. His opsonic index remaining at about 1, I postponed the second injection till October 13th, with the result that by this date a fresh peritoneal effusion had formed, and pleural dullness was returning. After the second injection ($\frac{1}{1000}$ mg.) the signs again began to subside, so that by October 24th there was no longer any evidence of ascites, and the pleurisy had cleared; the remaining abdominal enlargement and resistance to palpation gradually improved till, by September 7th, the organs appeared to be quite normal. He has remained well since, and is steadily gaining weight.

Opsonic indices, 17. Injections, 8.

PHTHISIS.

Only one case of phthisis has been treated, and this patient was chosen not because she seemed suitable for tuberculin, but because no other treatment offered a chance of improvement. The disease was too advanced for sanatorium treatment, so tuberculin was given a trial. The patient has been seven months under treatment and has held her own; the physical signs are much as at first, but with fewer moist sounds in the lungs. Her weight at the present time is 4 st. 12 lb., and I think she is better nourished than at first, but unfortunately her weight was not taken at the outset.

CASE.

J. L., 12 years of age, had a history of twelve months' duration. There was finger-clubbing and involvement of the whole left lung and the apex of the right. Her index before injection was 1.1, 0.8, 1.15, 0.8 on four separate occasions. The first injection ($\frac{1}{1000}$ mg.) was given on July 20th, and $\frac{1}{1000}$ mg. at intervals since. In January her index to streptococcus was 1.15 and to staphylococcus 2.0. She was treated in the wards for the first five or six weeks, went to the convalescent home for a time, and has been treated as an out-patient since October.

Opsonic indices, 16. Injections, 8.

THE INFLUENCE OF ANTITUBERCULOUS SERUM ON THE OPSONIC INDEX.

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VERY encouraging reports have been made as to the value of Marmorek's antituberculous serum by a large number of Continental writers; indeed, in looking through the available literature, scarcely any entirely adverse verdicts are to be found. Some authors write enthusiastically in favour of the remedy. Thus Richer states that it

is a true antitoxin, and temporarily inhibits the growth of the bacilli; Frey calls it undoubtedly a specific antitoxin, and Ullmann holds that it is superior to all other remedies yet devised against tuberculosis. It seems, therefore, advisable that more extended trials should be made of the serum in this country, and that records of the results obtained should be published, so that more complete statistics may be available for estimating the true value of the remedy. The following brief communication deals with one point only in the action of the serum—namely, its effect on the opsonic index of the blood, since in so chronic a disease as tuberculosis only a prolonged course of treatment can afford a basis for definite conclusions as to the value of any remedy, and such a trial was impossible in the circumstances in which we were situated.

The patients selected for this trial were all suffering from advanced tuberculosis of the lungs. This was in accordance with advice kindly given by Dr. Marmorek himself, it being difficult to estimate the effects of any

remedy in early cases, which often improve wonderfully under open air and plentiful feeding alone. One of our cases was probably hopeless from the outset; the others appeared capable of improvement, but had made little or no progress while in hospital. They were all febrile cases, such being chosen in the hope that the effect of the serum might be rendered visible on the temperature chart. In accordance with the advice of Dr. Marmorek the most recent method of administration of the serum, rectal injection, was chiefly employed; but in one case subcutaneous administration was used as a control.

CASE I.

C. B., aged 18 years. Tuberculosis of the right upper lobe and of the whole of the left lung. Very ill, vomiting at times, and suffering from abdominal pain, weakness, and emaciation. Going downhill; practically a hopeless case. Serum was given per rectum in daily doses of 5 c.c. from August 27th to September 15th. The patient's temperature appeared to fall a little during the first part of the course, and he looked and felt better, the pain being at first less, but returning towards the

end. There was no change in the physical signs. The opsonic index, after the first few doses of serum, rose from 0.4 to about 1.5; it was maintained at this level so long as serum was being given, and for the week following the last dose. Shortly after discontinuing the serum the opsonic index fell, and the patient seemed to go downhill more rapidly, suffering from greater pain and from vomiting; weakness increased. A second course was begun on October 20th, and again there seemed some diminution of pain; but the improvement was not maintained, although the opsonic index was raised. The injections were discontinued on October 31st, and the disease made rapid progress. He died on November 19th, and at the autopsy there was found extensive abdominal tuberculosis in addition to the pulmonary disease.

CASE II.

T. G. C., male, aged 37. Tuberculosis of whole of right lung and of left upper lobe. The patient's temperature was somewhat irregular, generally reaching 99° F. to 100° F. in the evening. Serum was given rectally, as in the former case, from

September 17th to October 6th. The temperature became steady about October 6th, and there was some subjective improvement, but the physical signs remained unchanged. The opsonic index was raised from 0.8 to 1.15, and maintained there for some time; it fell, however, to its original level on October 4th, just before the end of the series of injections.

CASE III.

J. A., male, aged 50. Tuberculosis of whole left lung and of right upper lobe. Temperature very similar to that in the last case. Serum was administered from August 31st to September 19th. The opsonic index rose from 0.8 and continued to oscillate about 1.3 for five weeks; that is to say, for all the time during which serum was being given—namely, twenty days—and for a fortnight after the last dose had been injected. The temperature was unaffected, but seemed to become more irregular after the serum had been discontinued.

The patient's appetite seemed to improve under the treatment but he suffered from rectal irritation. He refused a second course of injections, saying that he was not strong enough.

CASE IV.

O. J. C. K., a boy, aged 10, was said to have been ill for seven years. On admission there were signs of tuberculosis of the upper and lower lobes of both lungs. His temperature was irregular, generally reaching 99° to 100° F. in the evening, and occasionally rising to 103° F. Serum was given by the rectum from September 7th to 27th. The temperature remained irregular, but gradually became more steady, and was practically normal from September 28th to October 4th. In order to see whether horse-serum, as such, had any effect on the tuberculo-opsonic index the boy received two injections of antidiphtherial serum (1 c.cm. = 500 units) on October 31st and on November 3rd. On November 13th he received per rectum 10 c.cm. of antistreptococcal serum. His temperature after October 27th remained normal, except during a few days from November 3rd to November 8th. He steadily advanced in general condition, and left the hospital considerably improved at the beginning of January, but with the physical signs unaltered. In this case the opsonic index was high (1.75) to start with; it fell somewhat while serum was being administered, and a week after the last dose fell below normal. From that point on it gradually rose. The antidiphtherial serum seemed to cause a fall followed by a considerable rise to a higher level, which was well maintained after the injection of antistreptococcal serum on November 13th.

How far these changes were due to the three doses of horse-serum it is difficult to say.

CASE V.

T. H. S., a man of 49, was admitted suffering from tuberculosis of the right upper lobe and of both lobes on the left side; he also had tuberculous laryngitis. His temperature was persistently above normal, but seldom reached 100° F. He suffered from much pain in the throat. With a view to testing the effect of serum on this symptom he received subcutaneous injections of serum from October 29th to November 8th. These were discontinued owing to a fall in the opsonic index. The pain diminished somewhat during the treatment. From November 14th to 24th rectal injections were administered. Again the pain seemed to lessen, but there was no change in the physical signs. The patient finally left the hospital unimproved. The number of estimations in this case was rather small, but subcutaneous injections of serum produced an alarming fall in the opsonic index; when

the injections were stopped the index soon rose again, but was not affected either way when serum was given daily by the rectum.

Although it is well known that, in phthisical patients, the tuberculo-opsonic index undergoes considerable variation from time to time, yet, when we analyse the results obtained in the five cases which we have had under treatment, we come to the conclusion that a series of daily doses of Marmorek's antituberculous serum will, when administered rectally, usually produce a rise in the tuberculo-opsonic index; this rise begins after the first three or four doses and soon reaches a maximum, close to which the index remains for three or four weeks, while serum is being given, and does not fall till nearly a week after injections have been omitted. This rise in the opsonic index is coincident in some cases with an improvement in the general condition of the patient and a diminution of the diurnal variation of the temperature. Subcutaneous injections of the serum do not seem to have such a good effect; possibly a series of such injections given at longer intervals might be preferable as avoiding an accumulation of negative phases.

In order to see if other serums would have a similar effect, we tried giving antidiphtherial serum subcutaneously; the result was very much the same, in that it caused a rise in the tuberculo-opsonic index, but in this case an initial fall was observed; a rectal dose of antistreptococcal serum, given during this rise, did not seem to affect the index either way. It would be interesting to see in what way, if any, injections of normal horse-serum would affect the tuberculo-opsonic index.

If, as is suggested by our own experience, a rise in the index is produced by the administration of Marmorek's serum, but is not maintained for long after the serum has been omitted, the action of the serum might be explained by its containing an excess of opsonins. This, however, is scarcely to be expected, as a serum, when kept *in vitro*, gradually loses its opsonic power, so that at the end of two weeks the index is only about an eighth part of what it was when the serum was fresh. To prove that Marmorek's serum is not loaded with opsonins we tested its opsonic index in the usual way; in the slide made from normal serum we found 568 tubercle bacilli in 200 polymorphonuclear leucocytes, and in the slide made from Marmorek's serum only 72. This gives an index of 0.127. Some other explanation, therefore, must be found for the action of Marmorek's serum.

Should the conclusions which we have tentatively deduced from the small number of observations here recorded be confirmed by others, one piece of definite pathological evidence will have been furnished in support of the opinion of Continental writers, founded on clinical investigations, as to the remedial value of Marmorek's serum in tuberculosis. It seems highly desirable that

further investigation should be made as to the action of this preparation.

We are much indebted to Dr. Eyre for affording us every facility for carrying out the opsonic estimations in the Bacteriological Laboratory at Guy's Hospital.

THE RELATIVE OPSONIC POWER OF THE MOTHER'S BLOOD SERUM AND MILK.

BY

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OUR attention was first called to the question of the relative opsonic power of the blood serum and the milk of the human mother and of the cow by the statement of Professor Sims Woodhead at the Pathological Section of the British Medical Association at Toronto, that he had found opsonins corresponding to complement in cow's milk, and also opsonins of a somewhat different character the result of the injection of tuberculin.

To investigate this subject we estimated the opsonic index to the tubercle bacillus and to the *Staphylococcus pyogenes aureus* of (1) the mother's blood serum, (2) the mother's milk, (3) the blood serum of healthy cows, (4) the same cow's milk, and (5) the ordinary domestic milk supplied by the dairy company.

The usual method of Wright for estimating the opsonic index was used, and we employed our own white blood corpuscles, as we found those of the cow awkward to procure and difficult to work with. The normal standard was our own "pooled" blood serums. The mother's milk was obtained by means of a breast pump, at the same time as the blood was collected. Each cow was milked, and the blood was taken in one of Wright's tubes, by making a small incision into the cow's ear.

In order to obtain the "milk serum," one of the blood-collecting tubes was filled with the milk, and both ends sealed up. It was then centrifugalized until the cream was completely separated. The tube was marked with a file and broken into two parts; the milk serum could then be used quite free from fat.

All the women were healthy and were suckling healthy children.

Mother No. 1 was a primipara, aged 22 years, and the opsonic indices were estimated on the eighteenth day after parturition.

Mother No. 2 was a multipara, aged 24 years, suckling her third child. Blood and milk were examined in the ninth week after parturition.

Mother No. 3, aged 27, was suckling her fourth child. The opsonic estimations were made in the eleventh week after parturition.

The cows were all perfectly healthy, and were certified by a veterinary surgeon as free from tuberculous disease, though no tuberculin test was used. All these cows had calved within the last five or six months. The ordinary domestic milk supply which was examined was that obtained from a city dairy company, and its source was unknown. The saline solution used for the white corpuscles and for the emulsions of the organisms contained 0.85 per cent. of sodium chloride. The results of the opsonic estimations are given in the accompanying table.

It would appear from these figures that whilst the opsonic power of the mothers' blood serum for both the tubercle bacillus and the *Staphylococcus pyogenes aureus* is within the normal range, that of the milk from the same source is very low, averaging 0.077 for the tubercle bacillus and 0.11 for the *Staphylococcus pyogenes aureus*.

The cows' blood serum would appear to have about half the opsonic power of human blood—an average of 0.49 for the tubercle bacillus, and rather more than this, 0.71, for the *Staphylococcus aureus*. The index of the three cows' milk averaged about 0.25 for the tubercle bacillus and 0.18 for the staphylococcus, whilst the ordinary dairy supply averaged 0.20 and 0.05 for the same organisms respectively.

The presence of antitoxin has been demonstrated in the milk of animals immunized against various toxins, as, for example, the tetanus and diphtheria toxins. It has also been shown that the milk of animals immunized against

	Tuberculo-opsonic Index compared to Normal Human Serum.	Staphylococcic Tuberculo-opsonic Index compared to Normal Human Serum.
Blood Serum: Mother No. 1 ...	1.17	0.92
" " " No. 2 ...	1.10	0.98
" " " No. 3 ...	0.92	0.86
" " Cow No. 1 ...	0.45	0.72
" " " No. 2 ...	0.49	0.85
" " " No. 3 ...	0.53	0.55
Milk: Mother No. 1 ...	0.10	0.14
" " No. 2 ...	0.07	0.09
" " No. 3 ...	0.06	0.10
" Cow No. 1 ...	0.40	0.30
" " No. 2 ...	0.12	0.09
" " No. 3 ...	0.22	0.14
" Dairy Supply No. 1 ...	0.22	0.02
" " " No. 2 ...	0.19	0.09

the typhoid bacillus, and of mothers who have suffered from typhoid fever, contains agglutinins for that organism.

It would appear, however, that the amount of these protective substances in the milk is very much less than in the blood, being usually about in the ratio of 1 to 30, in the case of antitoxin.

With the object of comparing the opsonic power of the blood serum of the child with that of the mother's serum and milk, we estimated the opsonic index of the blood of two newly-born children for the same two organisms, and obtained the following result:

	Tuberculo-opsonic Index compared to Normal Serum.	Staphylococcic Opsonic Index compared to Normal Serum.
Mother's blood serum, No. 1 ..	1.09	0.90
Child's blood serum, No. 1 (estimated on 7th day after birth) ..	0.72	0.55
Mother's blood serum, No. 2 ...	1.16	—
Child's blood serum, No. 2 (estimated on 4th day after birth) ..	0.40	—

It will be seen that in both these cases the opsonic power of the child's blood is very much less than that of the mother, and it would be interesting to know whether any absorption of opsonins can take place from the mother's milk. The opinion of authorities seems to be divided on the question of the absorption or not of agglutinins and antitoxins in the intestinal canal of the child.

Another aspect of the question which it would be of interest to investigate is the opsonic content of the milk of mothers and of cows suffering from tuberculosis. If there are tubercle bacilli in the milk we can conceive of these uniting themselves to, or combining with, the opsonin present, and thus becoming capable of absorption by the phagocytes in the intestinal walls. If there is enough opsonin present, will the bacilli become comparatively harmless; or, on the other hand, if the opsonic power of the milk is small, would the admixture of milk rich in opsonin be a means of rendering the milk less harmful?

ANTITOXIN FROM CONVICTS.—We learn from the *Medical Record* that at a recent meeting of the Baltimore County Medical Association, Dr. H. Burton Stevenson said that antitoxins would be more effective if they were prepared in the human body, because only a few animals were susceptible to the diseases of man. He suggested that such antitoxin could readily be produced by using criminals for the production of serums. A law could be enacted making the punishment for certain crimes optional with the convict—imprisonment on the one hand, inoculation with certain disease germs on the other.